Remarks

Restriction Requirement/Election of Species

Applicants hereby affirm their election of Group IV, claims 12-15.

Amendment of claims

All claims withdrawn due to the restriction requirement (claims 1-11, 16-22) are hereby canceled. Claim 12 is amended to delete unnecessary language from the preamble of the claim, and to incorporate the limitations of claim 15. New claims 23-25 are supported in the specification at p. 40 (specific induction of hMUC2) and pp. 25-28 (design of screening assays).

Rejection Under §112, 1st Paragraph

Claims 12-15 were rejected as lacking enablement and written description under §112, 1st paragraph. Applicants respectfully traverse.

Applicants submit that both the enablement and the written description rejections are rendered moot by the amendments above, which limit the pending claims to hCLCA1 and delete "fragment" language. With regard to description of hCLCA1, Applicants point out that hCLCA1 was already sequenced and published at the time the application was filed (see A.D. Gruber et al., Genomics (1998) 54:200-14, reference AH).

Rejection Under §102(b)

A. Gandhi et al.

Claims 12-14 were rejected as anticipated under §102(b) over R. Gandhi et al., J Biol Chem (1998) 48:32096-101, reference AG ("Gandhi"). Applicants respectfully traverse.

Gandhi disclosed the cloning and expression of the mouse protein mCLCA1. Gandhi noted that the sequence identity between mCLCA1 and hCLCA1 is only 53% (see Gandhi, p. 32097, col. 2), and that mCLCA1 is expressed "in a wide variety of tissues", finding expression in spleen, kidney, lung, liver, and brain (Gandhi, p. 32098, col. 2).

> "The tissue expression patterns of bCLCA1, Lu-ECAM-1, hCLCA1, and mCLCA1 are quite different. ... This heterogeneity in tissue expression suggests differences in function, regulation, and associated disease among the various members of a structurally distinct family of chloride channels." (Gandhi at p. 32100.)

As noted above, the claims have been amended to claim the use of hCLCA1. As hCLCA1 and mCLCA1 are distinctly different proteins, Gandhi fails to anticipate the claimed invention.

B. Gruber et al.

Claims 12-15 were rejected as anticipated under §102(b) over A.D. Gruber et al., Genomics (1998) 54:200-14, reference AH, ("Gruber"). Applicants respectfully traverse.

Gruber disclosed the sequence and expression of hCLCA1, including expression in HEK cells and exposure to DIDS, DTT, niflumic acid, and ionomycin with resulting changes in the Ca^{2+}-sensitive Cl^- current (Gruber at p. 201, col. 2).

However, although Gruber suggested that "human CLCA1 ... may be involved in secretory or absorptive processes" (Gruber at p. 210, col. 2), Gruber failed to show any link between hCLCA1 and mucin regulation. Thus, Gruber failed to anticipate the method of screening for modulators of mucin expression or mucus secretion, as claimed herein.

Applicants respectfully submit that the application is now in condition for allowance, and solicit such action at an early date. If there are any remaining questions, the Examiner is invited to telephone the undersigned at the numbers provided below.

Respectfully submitted,

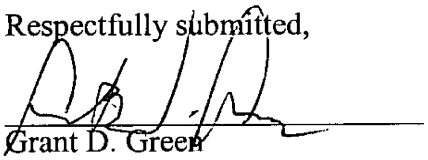

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Table I.

Gene name	GenBank Accession #	Forward Primer	Reverse Primer	Taqman Probe
hGAPDH	M33197	GTTCGACAGTCAGCCGCATC SEQ ID NO:1	GGAATTTGCCATGGGTGGA SEQ ID NO:2	ACCAGGCGCCCAATACGACCAA SEQ ID NO:3
hMUC1	AF084521	GCCAGGATCTGTGGTGGTACA SEQ ID NO:4	CTCCACGTCGTGGACATTGA SEQ ID NO:5	GGCACATCACTCACGCTGACGTCTGA SEQ ID NO:6
hMUC2	L21998	CCCAACTTTGATGCCAGCATT SEQ ID NO:7	CAGCATCCATTGGGCATGA SEQ ID NO:8	TGTGATGGAGCCCGGGATGCA SEQ ID NO:9
hMUC4	AJ010901	CGAAAACAGCCCACTGATGTC SEQ ID NO:10	TGGAGGCCTGAGTTGGAATT SEQ ID NO:11	AGGGCGATACCTCTCCCACACTGGC SEQ ID NO:12
hMUC5AC	U06711	TACTCGCTCGAGGGCAACA SEQ ID NO:13	TGCAGTGCAGGGTCACATTC SEQ ID NO:14	CCAGGAGCTGCGGACCTCGC SEQ ID NO:15
hMUC5B	Z72496	GTGTGGGTGGTCTCTGGAGTAGA SEQ ID NO:16	AAATCCACAGCTACCAGCTTTACA SEQ ID NO:17	TGGACCGTCCCAGCACAGACCA SEQ ID NO:18
hMUC6	HSU97698	CCACTTCTGCCTCCATCCA SEQ ID NO:19	GGCCTTGAGCGTTGTTGGT SEQ ID NO:20	TCAACGCCAACAGGCACCGTTC SEQ ID NO:21
hCLCA1	AF039400	GCAAGGTGGCTTTGTAGTGGA SEQ ID NO:22	AGACTGTATTTCCAAGTGCCAACC SEQ ID NO:23	ACACCAAAATGGCCTACCTCCAAATCCC SEQ ID NO:24
hCLCA2	AF043977	GAGGCCGAGTGTTTGTCCAT SEQ ID NO:25	CCATTTATGTAGAAAGGTTTGTCATTG SEQ ID NO:26	TGGGCCCACCTCCGTTGGG SEQ ID NO:27
hCLCA3	AF043976	CCTGAAGTCACAGATGATGTGGAA SEQ ID NO:28	AGGCACTCCTGATACAGTAAACGA SEQ ID NO:29	CAGACGACTTCAGCAGACTCACCTCTGG SEQ ID NO:30
hCLCA4	AF127035	GAATCAAGCAGCAAAACATTTCC SEQ ID NO:31	GTGGCAGTACTATCAAAGTGAACCA SEQ ID NO:32	CCCAGGATCCATTTTCAACAGTCTGCAG SEQ ID NO:33
mGAPDH	M32599	GTCCCGTAGACAAAATGGTGAAG SEQ ID NO:34	GTGACCAGGCGCCCAAT SEQ ID NO:35	CGGTGTGAACGGATTTGGCCG SEQ ID NO:36

Appendix B

What is claimed:

12. A method of screening for a compound that modulates mucus secretion, the method comprising the steps of:

    a) contacting hCLCA1 with the compound; and

    b) detecting hCLCA1 activity.

13. The method of claim 12, wherein hCLCA1 is:

    a) expressed on a cell or tissue; or

    b) immobilized on a solid support.

14. The method of claim 12, wherein the compound is:

    a) an antagonist of hCLCA1 activity; or

    b) an agonist of hCLCA1 activity.

23. A method of screening for a compound that modulates mucin expression, said method comprising:

    a) contacting hCLCA1 with a compound; and

    b) detecting mucin expression or transcription.

24. The method of claim 23, wherein mucin transcription is detected using RT-PCR.

25. The method of claim 23, wherein mucin transcription is detected using a reporter gene operably linked to an hMUC2 promoter.